New medication given every one to three months may slash stubborn high cholesterol

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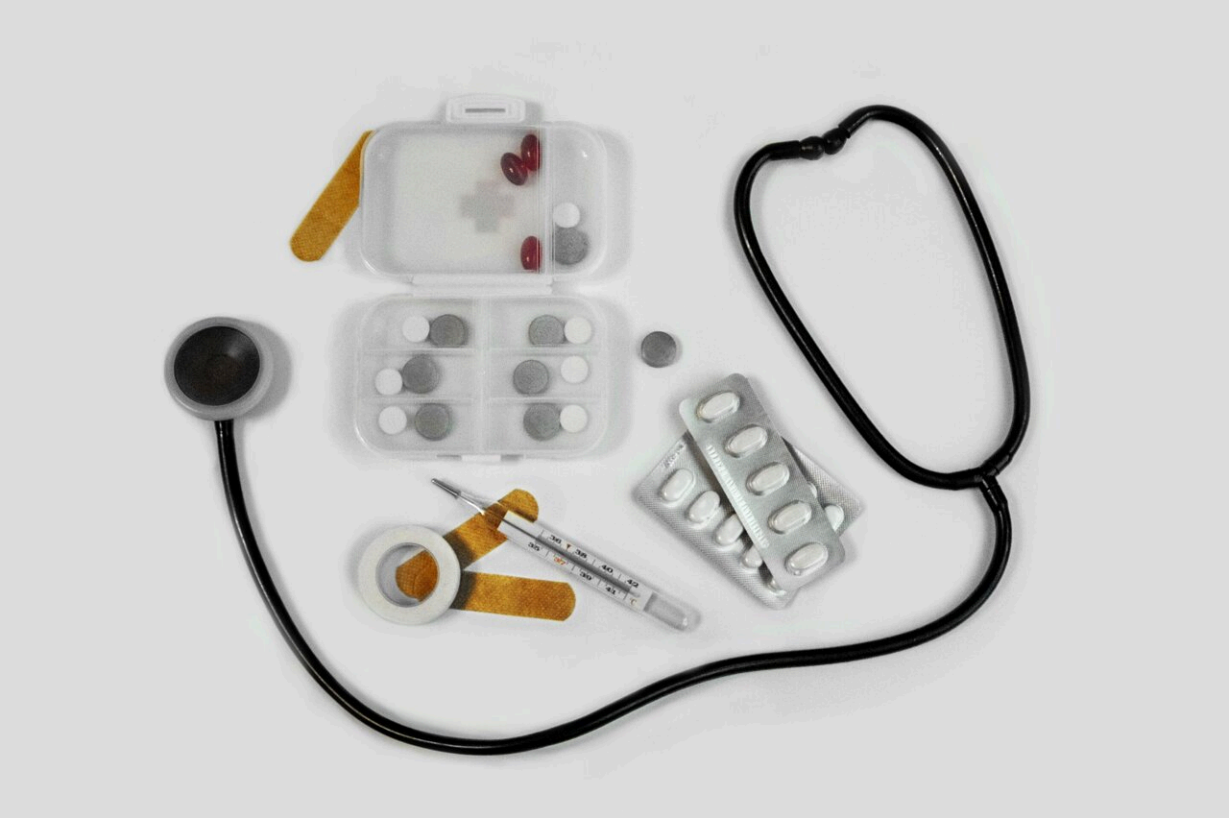

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A new PCSK9 inhibitor (recaticimab) injected every one to three months may work safely and provide more flexible dosing to lower cholesterol, according to late-breaking science presented today at the

American Heart Association's Scientific Sessions 2023. The meeting, held Nov. 11–13, in Philadelphia, is a premier global exchange of the latest scientific advancements, research and evidence-based clinical practice updates in cardiovascular science.

"Previous studies found that 30% to 40% of people discontinued their current PCSK9 therapies, given every two to four weeks, during or after six months of beginning treatment. More flexible dosing with recaticimab, given up to every 12 weeks, might increase the proportion of people with high levels of bad cholesterol to stick with their recommended treatment to lower bad cholesterol levels and reduce risk of heart disease," said lead study author Xin Du, Ph.D., a professor of cardiology at Beijing Anzhen Hospital and the Capital Medical University in Beijing, China.

The current study, "Recaticimab Add-On Therapy in Patients With Non-Familial Hypercholesterolemia and Mixed Hyperlipidemia or REMAIN-2," examines the safety of a new PCSK9 inhibitor, recaticimab, and its ability to lower bad cholesterol when given at different doses and intervals to people with non-genetic forms of high cholesterol.

American Heart Association guidelines indicate a cholesterol target of less than 100 mg/dl in most adults and less than 70 mg/dl in high-risk people who have already had a heart attack, or stroke or have genetic forms of high cholesterol. When cholesterol-lowering statin medications and other treatments are not effective in reducing bad cholesterol to target levels, physicians may often add a PCSK9 inhibitor. The medication binds to and inactivates a protein on cells found in the liver to lower bad cholesterol. Current FDA approved PCSK9 inhibitors include alirocumab and evolocumab, which are injected every 2–4 weeks.

This multicenter study in China involved 689 participants with abnormally high levels of bad cholesterol despite ongoing moderate or high intensity statin therapy. Participants were divided into three groups: one received either 150 mg of recaticimab or a placebo injection every four weeks; one group received 300 mg of recaticimab or placebo injection every eight weeks; and one group was given 450 mg of recaticimab or placebo injection every 12 weeks.

The study found:

- At every dosage/interval, participants who received recaticimab had lower bad cholesterol levels at 24 weeks than those receiving a placebo.
- In the 4-week injection group, bad cholesterol was reduced 62% among those taking recaticimab vs. 0% among those in the placebo group; in the 8-week injection group, bad cholesterol was reduced 59% vs. +0.4% respectively; and in the 12-week injection group bad cholesterol was reduced 51% vs. +2% respectively.
- At every dosage/interval, recaticimab lowered their bad cholesterol to the target by 24 weeks compared to the placebo and these levels were maintained at 48 weeks.
- At 24 weeks, 90% of the 4-week injection group reached goal compared to 16% of the placebo group; while the percentage was 95% vs. 14% respectively in the 8-week injection group; and 86% vs. 16% respectively in the 12-week injection group.
- A similar amount of injection site reactions were common during the 48 weeks, such as: redness and soreness was 84% for those on recaticimab and 83% for those on placebo; injection site reaction was 3.9% in the recaticimab and 1.3% in the placebo groups.

"Since all the doses and frequencies had similar effectiveness and safety,

this may someday provide patients and physicians with more flexible options," Du said.

In the study's secondary findings, other types of lipids associated with atherosclerotic heart disease were also reduced significantly in the recaticimab groups compared to the placebo groups, including:

- Lipoprotein(a), or Lp(a), a type of cholesterol inherited from family that is a common independent risk factor for heart disease, dropped 29%–40% in the recaticimab groups versus decreases of 0.1%—9.5% in the placebo groups;
- Apolipoprotein B, a component of proteins of very low-, low-density and intermediate-density lipoproteins, were down 42%–53% in the recaticimab groups versus increases of 0.3%–2.5% in the placebo groups; and
- A measure of all cholesterol content—except the "good cholesterol" known as high-density lipoprotein cholesterol—were down 44%–55% in the recaticimab groups versus increases of 1%–4% in the placebo groups.

"Recaticimab reduced these key lipid parameters by a similar magnitude to other PCSK9 inhibitors, providing further evidence of profound benefits with the treatment despite less frequent dosing," Du said.

Trial background and details:

- The study was conducted between June 2021 and March 2023, the average age of participants was about 56-years-old and 64% were men.
- About 69% of participants had existing thickening or hardening of the arteries, and all had abnormally high levels of bad cholesterol (more than 70 mg/dl for those with cardiovascular disease and more than 100 mg/dl for those without) despite

ongoing moderate- or high-intensity statin therapy.
- REMAIN-2 was a multicenter, randomized, double-blind, placebo-controlled, phase 3 trial which means neither the participants or the researchers were aware of who was assigned to each group.

Although there are several statin medications, all participants in this study were taking either atorvastatin or rosuvastatin, so the impact of adding recaticimab to other statins may differ, researchers note. In addition, because the study was conducted in China, where a higher proportion of people often have increased rates of reactions and intolerance to statin treatment, more of the participants were on moderate rather than high intensity statin therapy, and the results may not be generalizable to other populations. In addition, changes in laboratory measures in this study suggest but do not demonstrate that recaticimab add-on treatment may lower rates of heart attack and stroke, Du said.

"Further studies will be conducted to explore the possible benefits of recaticimab in reducing cardiovascular risk," Du said.

In addition, a separate trial, REMAIN-3, is being completed to determine whether recaticimab reduces bad cholesterol in people who have one gene for familial hypercholesterolemia, a genetic disorder that causes high low-density-lipoprotein cholesterol and increases the risk for developing heart disease or having a heart attack at a younger age.

More information: Recaticimab Add-On Therapy in Patients With Non-Familial Hypercholesterolaemia and Mixed Hyperlipidemia (REMAIN-2): A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 3 Trial. www.abstractsonline.com/pp8/?_ … 1/presentation/16573

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